THE SYNTHESIS OF SOME PHENYL SUBSTITUTED ALIPHATIC DICARBOXYLIC ACIDS RELATED TO STRUCTURE STUDIES OF GR-S

BY

ALLEN CHARLTON MOORE

A. B., University of Texas, 1937

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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Introduction

An important approach to determining the total structure of the GR-S copolymer has been the use of degradation procedures, chief among which has been ozonolysis.[1,2] The object of such an approach was to cleave the chain at points of unsaturation, then to isolate and identify the fragments, which consisted primarily of aliphatic polycarboxylic acids. By a study of the water-soluble acids it has been possible to account for up to 97 per cent of the butadiene units of the polymer chain. Investigation of the water-insoluble fraction, which contained most of the styrene units, has been hampered by the difficult task of isolating and identifying the more complex acids. It was reported[2] that a diphenylsuberic acid was the principal constituent of this fraction, however, it was not possible to complete the identification for lack of an authentic sample for comparison. The purpose of the present work was to prepare β, δ-diphenylsuberic acid in order to facilitate identification of the acid previously isolated, thus clarifying an important aspect of the structure of GR-S.

Discussion of Results

In the first three plans for the synthesis, attempts were made to apply the Reformatsky condensation to γ- and δ-keto esters to obtain dibasic esters from which the desired β, δ-diphenylsuberic acid could then be derived. Thus, in the first scheme, ethyl β, δ-diphenylpimelate was to be prepared by the reaction of ethyl β-phenyl-γ-benzoylbutyrate with ethyl bromoacetate; in the second plan, ethyl α,γ-diphenyl-γ-hydroxyadipate was to be made from ethyl α-phenyl-β-benzoylpropionate and ethyl bromoacetate; and in the third

scheme, the desired carbon chain was to be obtained directly by the condensation of ethyl β-benzoylpropionate with ethyl β-phenyl-γ-bromocrotonate. However, in none of these cases was the Reformatsky reaction successful.

The fourth approach to the problem, a more flexible one, was by way of a cyclic intermediate, 3,5-diphenylcyclohexene (I). It was planned to prepare this compound from the cyclic adduct obtained by the Michael condensation of dibenzalacetone and ethyl cyanoacetate. The product, ethyl 1-cyano-2,6-diphenyl-4-ketocyclohexane - 1 - carboxylate (II), was then to be hydrolyzed and decarboxylated to the corresponding keto nitrile. The keto acid obtained from this nitrile, after decarboxylation, hydrogenation, and dehydration should then give the desired unsaturated compound (I). By oxidation of this intermediate, α,γ-diphenyladipic acid would result, and from it, by simultaneous extension of the chain at either end by one carbon atom through the Arndt-Eisert reaction, the desired acid should then be obtained.

It was found that while the cyclic adduct (II) could be hydrolyzed to give fair yields of the free acid,[3] the subsequent decarboxylation step was not successful. Altering the original plan somewhat, the keto group of the adduct (II) was then reduced in the presence of aluminum isopropoxide, giving a 40 to 48 per cent yield of the δ-lactone (III) corresponding to the expected hydroxy ester. The remainder of the reduction product was a glassy resin from which, after hydrolysis, there was obtained a 63 per cent yield of 1-cyano-2,6-diphenyl-4-hydroxycyclohexane-1-carboxylic acid (IV). 1-Cyano-2,6-diphenyl-4-hydroxycyclohexane (V) was then prepared, in 80 per cent yield, by refluxing the δ-lactone (III) with 40 per cent aqueous sodium hydroxide for three hours. Decarboxylation of the free acid (IV) also gave this same hydroxy nitrile (V), in 50 per cent yield.

By refluxing the δ-lactone (III) with strong alkali for an additional twenty-eight hours, the hydroxy nitrile (V) was hydrolyzed and there was obtained 2,6-diphenyl-4-

hydroxycyclohexane-1-carboxylic acid (VI) in 94 per cent overall yield. Although this compound corresponded closely to the keto acid in the original scheme, all attempts to utilize it as an intermediate were unsuccessful, since it readily formed a δ-lactone (VII) when heated, or when treated with acetylating or methylating agents. These data indicated clearly that both the hydroxy nitrile (V) and the hydroxy acid (VI) were of *cis* configuration.

To eliminate the difficulty of lactonization it was then planned to tie up the hydroxyl group of the hydroxy nitrile (V) as an ether or ester, prior to its hydrolysis to the acid. Accordingly, the *cis*-methyl ether (VIII) of the hydroxy nitrile (V) was prepared, in 66 per cent yield. It was found, however, that this methoxy nitrile (VIII) could be hydrolyzed only with difficulty to the desired methoxy acid (IX). Consequently, it was not practical to continue this series and attempt preparation of 3,5-diphenylmethoxycyclohexane. An effort to prepare the *trans*-methoxy nitrile by inversion of the *p*-toluenesulfonic ester of the hydroxy nitrile (V) with sodium methoxide was not successful as it was possible to isolate only a small yield of 1-cyano-2,6-diphenylcyclohexene.

4-Acetoxy-1-cyano-2,6-diphenylcyclohexane, prepared in 85 per cent yield, proved to be of no value as an intermediate, since its hydrolysis by alkali gave the δ-lactone (VII). 4-Chloro-1-cyano-2,6-diphenylcyclohexane was also prepared, but the yield was too small to make practical its further investigation as a possible intermediate.

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VITA

The author was born on November 22, 1915, in Houston, Texas. He attended the public schools of that city and was graduated from Reagan High School in 1933. He received the Bachelor of Arts degree in chemistry at the University of Texas in 1937, then accepted employment as junior chemist with the City of Houston. From 1939 to 1941 he taught high school chemistry in the public schools of Kerrville, Texas. Returning to the University of Texas, he completed the Master of Arts degree in organic chemistry in 1943. After a brief period as Assistant Professor of Chemistry in the Army Specialized Training Program at The Citadel, Charleston, S. C., he accepted a position as research chemist with the Development Department of the West Virginia Pulp and Paper Company, of the same city. In October, 1945, he enrolled in the Graduate College of the University of Illinois and held a special research assistantship in the Government Rubber Research Program, a position in which he continued until the time of his graduation in 1948. He is the co-author of one publication, "Dehydrochlorination of 3-Chloro-2-propen-1-ol: Preparation of Propargyl Alcohol," J. Am. Chem. Soc., **66,** 285 (1944).

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